IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Irun R. COHEN et al.	Confirmation No.: 5950
Patent No.: 7,118,744 B2	Application No.: 10/032,482
Patent Date: October 10, 2006	Filing Date: January 2, 2002
For: IMMUNOGENIC COMPOSITIONS FOR INDUCTION OF ANTI-TUMOR IMMUNITY	Attorney Docket No.: 85189-700

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentees hereby respectfully request the issuance of a Certificate of Correction in connection with the above-identified patent. The corrections are listed on the attached Form PTO-1050. The corrections requested are as follows:

Title Page:

Item (56) **References Cited**, OTHER PUBLICATIONS, Lee et al. reference, after "DNA damage in the form of insertion/" delete "deletin" and insert -- deletion --. Support for this change appears on applicants' PTO/SB08A filed January 2, 2002.

Column 29:

Line 61 (claim 1, line 2), after "p53, which peptide is 7 to 30 amino" delete "acids" and insert -- acid residues --.

Line 63 (claim 1, line 4), after "of a CDR of the heavy" delete "chain".

Support for the above changes appear in application claim 8.

Column 31:

Line 27 (claim 7, line 8), after "Asn-Tyr-Asn-Gln-" insert -- Asn- --.

Line 57 (claim 7, line 20), after "Ser-" delete "Phr" and insert -- Phe --.

Line 61 (claim 7, line 23), after "(421 VH), and peptide IVc containing the" delete "DCR3" and insert --CDR3 --.

Support for the above changes appear in application claim 19.

Column 32:

Line 48 (claim 11, line 30), after "(IVc) Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr (SEQ ID NO:20)" delete "." and insert -- ; --. Support for this change appears in application claim 24

The requested corrections are for errors that appear to have been made by the Office. Therefore, no fee is believed to be due for this request. Should any fees be required, however, please charge such fees to Winston & Strawn LLP Deposit Account No. 50-1814. Please issue a Certificate of Correction in due course.

Respectfully submitted,

10/31/06
Date

Allan A. Fanucci, Reg. No. 30,256

WINSTON & STRAWN LLP
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212-294-3311

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO.: 7,118,744 B2
APPLICATION NO.: 10/032,482
DATED: Oct. 10, 2006
INVENTOR(S): Cohen et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page:
Item (56) **References Cited**, OTHER PUBLICATIONS, Lee et al. reference, after "DNA damage in the form of insertion/" delete "deletin" and insert -- deletion --.

Column 29:
Line 61, after "p53, which peptide is 7 to 30 amino" delete "acids" and insert -- acid residues --.
Line 63, after "of a CDR of the heavy" delete "chain".

Column 31:
Line 27, after "Asn-Tyr-Asn-Gln-" insert -- Asn- --.
Line 57, after "Ser-" delete "Phr" and insert -- Phe --.
Line 61, after "(421 VH), and peptide IVc containing the" delete "DCR3" and insert --CDR3 --.

Column 32:
Line 48, after "(IVc) Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr (SEQ ID NO:20)" delete "." and insert -- ; --.

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(12) **United States Patent**
Cohen et al.

(10) **Patent No.: US 7,118,744 B2**
(45) **Date of Patent: Oct. 10, 2006**

(54) **IMMUNOGENIC COMPOSITIONS FOR INDUCTION OF ANTI-TUMOR IMMUNITY**

(75) Inventors: **Irun R Cohen**, Rehovot (IL); **Varda Rotter**, Rishon LeZion (IL); **Roland Wolkowicz**, Redwood City, CA (US); **Pedro Ruiz**, Stanford, CA (US); **Neta Erez-Alon**, Tel Aviv (IL); **Johannes Herkel**, Wuerzberg (DE)

(73) Assignee: **Yeda Research and Development Co., Ltd.**, Rehovot (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 259 days.

(21) Appl. No.: **10/032,482**

(22) Filed: **Jan. 2, 2002**

(65) **Prior Publication Data**

US 2002/0197270 A1 Dec. 26, 2002

Related U.S. Application Data

(62) Division of application No. 09/445,602, filed as application No. PCT/IL98/00266 on Jun. 9, 1998, now abandoned.

(30) **Foreign Application Priority Data**

Jun. 9, 1997 (IL) 121041

(51) **Int. Cl.**
A61K 39/395 (2006.01)
C07P 16/00 (2006.01)
C12P 21/08 (2006.01)

(52) **U.S. Cl.** **424/141.1**; 424/130.1; 424/133.1; 530/387.1; 530/388.1

(58) **Field of Classification Search** 530/300, 530/350, 387.1, 387.2; 424/184.1
See application file for complete search history.

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deletion

(Continued)

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(57) **ABSTRACT**

The invention relates to the use of an immunogen selected from the group consisting of

(i) an anti-p53 mAb;
(ii) a fragment of an anti-p53 mAb;
(iii) a peptide based on a CDR of the heavy or light chain of an anti-p53 mAb, which peptide is capable of eliciting antibodies to p53; and
(iv) a DNA molecule coding for the variable (V) region of an anti-p53 mAb in a suitable gene delivery vehicle, for the preparation of a pharmaceutical composition useful for induction of anti-tumor immunity in mammals, for activating an enhanced immune response to a p53 molecule in mammals, and/or for induction of immune responses to mutated and wild-type forms of a p53 in mammals. The use of anti-p53 mAbs and novel peptides based on the CDR2 and CDR3 of the heavy chains and CDR3 of the light chains of different anti-p53 mAbs are disclosed.

15 Claims, 5 Drawing Sheets

-continued

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What is claimed is:

1. A synthetic peptide capable of eliciting antibodies to p53, which peptide is 7 to 30 amino acids in length of a variable region of an anti-p53 mAb and contains a sequence of a CDR of the heavy chain or light chain of the anti-p53 mAb, and salts thereof, wherein the sequence of the CDR is selected from the polypeptide sequences of mAb 240, mAb 246 and mAb 421.

acid residues

2. A synthetic peptide according to claim 1, containing a sequence of the CDR2 or CDR3 of the heavy chain, or of the CDR3 of the light chain, of an anti-p53 mAb.

3. A synthetic peptide according to claim 1, wherein the peptide contains a sequence selected from the group of sequences consisting of Ic (SEQ ID NO:11), IIa (SEQ ID NO:12), and IVc (SEQ ID NO:20).

4. A synthetic peptide according to claim 3, wherein the peptides are selected from the group consisting of peptides V–VII of the sequences:

Peptide V: Tyr-Tyr-Cys-Gln-His-Ile-Arg-Glu-Leu-Thr-Arg-Ser-Glu-Gly-Gly-Pro-Ser (SEQ ID NO:21),

Peptide VI: Gly-Val-Tyr-Tyr-Cys-Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr-Phe-Gly-Ala-Gly-Thr-Lys (SEQ ID NO:22),

Peptide VII: Gly-Asp-Ile-Asn-Pro-Asn-Asn-Gly-Tyr-Thr-Ile-Tyr-Asn-Gln-Lys-Val-Lys-Gly-Lys-Ala (SEQ ID NO:23), and salts thereof.

5. A synthetic peptide according to claim 1, wherein the peptide contains the sequence: Gln-His-Ile-Arg-Glu-Leu-Thr-Arg (SEQ ID NO:11) or Tyr-Tyr-Cys-Gln-His-Ile-Arg-Glu-Leu-Thr-Arg-Ser-Glu-Gly-Gly-Pro-Ser (SEQ ID NO:21).

6. The peptide of claim 1 in the form of an organic or inorganic salt thereof.

7. The peptide of claim 2, wherein the peptide is selected from the group consisting of:

(i) peptides, herein designated Ia–Ib, containing the CDR2 and CDR3, respectively, of the heavy chain (240VH), and peptide Ic containing the CDR3 of the light chain (240VL), of the anti-p53 mAb 240, of the sequences: (Ia) Glu-Ile-Asp-Pro-Ser-Asp-Ser-Tyr-Thr-Asn-Tyr-Asn-Gln-Phe-Lys-Asp (SEQ ID NO:9), (Ib) Leu-Leu-Arg-Tyr-Phe-Ala-Met-Asp-Tyr (SEQ ID NO:10), or (Ic) Gln-His-Ile-Arg-Glu-Leu-Thr-Arg (SEQ ID NO:11);

(ii) peptides, herein designated IIa–IIb, containing the CDR2 and CDR3, respectively, of the heavy chain (246VH), and peptide IIc containing the CDR3 of the light chain (246VL), of the anti-p53 mAb 246, of the sequences: (IIa) Asp-Ile-Asn-Pro-Asn-Asn-Gly-Tyr-Thr-Ile-Tyr-Asn-Gln-Lys-Val-Lys-Gly (SEQ ID NO:12), (IIb) Gly-Gly-Gly-Leu-Lys-Gly-Tyr-Pro-Phe-Val-Tyr (SEQ ID NO:13), or (IIc) Gln-Gln-Arg-Ser-Ser-Phe-Pro-Phe-Thr (SEQ ID NO:14);

(iii) peptides, herein designated IVa–IVb, containing the CDR2 and CDR3, respectively, of the heavy chain (421VH), and peptide IVc containing the CDR3 of the light chain (421VL), of the anti-p53 mAb 421, of the sequences: (IVa) Trp-Ile-Asp-Pro-Glu-Asn-Gly-Asp-Thr-Glu-Tyr-Ala-Pro-Lys-Phe-Gln-Gly (SEQ ID NO:18), (IVb) Tyr-Gly-Asp-Ala-Leu-Asp-Tyr (SEQ ID NO:19), or (IVc) Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr (SEQ ID NO:20); and salts thereof.

8. A pharmaceutical composition comprising the peptide of claim 1 and a pharmaceutically acceptable carrier.

9. The pharmaceutical composition of claim 8, wherein the peptide contains a sequence of the CDR2 or CDR3 of the heavy chain, or of the CDR3 of the light chain, of an anti-p53 mAb.

10. The pharmaceutical composition of claim 9, wherein the peptide contains the sequence: Gln-His-Ile-Arg-Glu-Leu-Thr-Arg (SEQ ID NO:11) or Tyr-Tyr-Cys-Gln-His-Ile-Arg-Glu-Leu-Thr-Arg-Ser-Glu-Gly-Gly-Pro-Ser (SEQ ID NO:21).

11. The pharmaceutical composition of claim 8, wherein the peptide is selected from the group consisting of:

(i) peptides, herein designated Ia–Ib, containing the CDR2 and CDR3, respectively, of the heavy chain (240VH), and peptide Ic containing the CDR3 of the light chain (240VL), of the anti-p53 mAb 240, of the sequences: (Ia) Glu-Ile-Asp-Pro-Ser-Asp-Ser-Tyr-Thr-Asn-Tyr-Asn-Gln-Asn-Phe-Lys-Asp (SEQ ID NO:9), (Ib) Leu-Leu-Arg-Tyr-Phe-Ala-Met-Asp-Tyr (SEQ ID NO:10), or (Ic) Gln-His-Ile-Arg-Glu-Leu-Thr-Arg (SEQ ID NO:11);

(ii) peptides, herein designated IIa–IIb, containing the CDR2 and CDR3, respectively, of the heavy chain (246VH), and peptide IIc containing the CDR3 of the light chain (246VL), of the anti-p53 mAb 246, of the sequences:

(IIa) Asp-Ile-Asn-Pro-Asn-Asn-Gly-Tyr-Thr-Ile-Tyr-Asn-Gln-Lys-Val-Lys-Gly (SEQ ID NO:12),

(IIb) Gly-Gly-Gly-Leu-Lys-Gly-Tyr-Pro-Phe-Val-Tyr (SEQ ID NO:13), or

(IIc) Gln-Gln-Arg-Ser-Ser-Phe-Pro-Phe-Thr (SEQ ID NO:14);

(iii) peptides, herein designated IVa–IVb, containing the CDR2 and CDR3, respectively, of the heavy chain (421VH), and peptide IVc containing the CDR3 of the light chain (421VL), of the anti-p53 mAb 421, of the sequences:

(IVa) Trp-Ile-Asp-Pro-Glu-Asn-Gly-Asp-Thr-Glu-Tyr-Ala-Pro-Lys-Phe-Gln-Gly (SEQ ID NO:18),

(IVb) Tyr-Gly-Asp-Ala-Leu-Asp-Tyr (SEQ ID NO:19), or

(IVc) Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr (SEQ ID NO:20);

and salts thereof.

12. The pharmaceutical composition of claim 8, wherein the peptide contains a sequence selected from the group of sequences consisting of Ic (SEQ ID NO:11), IIa (SEQ ID NO:12), and IVc (SEQ ID NO:20).

13. The pharmaceutical composition of claim 12, wherein the peptides are selected from the group consisting of peptides V–VII of the sequences:

Peptide V: Tyr-Tyr-Cys-Gln-His-Ile-Arg-Glu-Leu-Thr-Arg-Ser-Glu-Gly-Gly-Pro-Ser (SEQ ID NO:21),

Peptide VI: Gly-Val-Tyr-Tyr-Cys-Trp-Gln-Gly-Thr-His-Ser-Pro-Leu-Thr-Phe-Gly-Ala-Gly-Thr-Lys (SEQ ID NO:22),

Peptide VII: Gly-Asp-Ile-Asn-Pro-Asn-Asn-Gly-Tyr-Thr-Ile-Tyr-Asn-Gln-Lys-Val-Lys-Gly-Lys-Ala (SEQ ID NO:23), and salts thereof.